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Augmented Renal Clearance in Iranian Critically Ill Patients: Retrospective Study at Masih Daneshvari Hospital

Seyed Reza Saghebi [1], Behrooz Farzanegan [1], Payam Tabarsi [2], Rokhsaneh Zangooi [3], Batoul Khoundabi [4], Naghmeh Ahmadi [3], Shirin Shams [3], Farhad Salari [3], Mehdi Golpayegani [3] and Seyed Mohammad Reza Hashemian [3, *]

[1] Tracheal Diseases Research Center, National Research Institute of Tuberculosis and Lung Diseases (NRITLD), Shahid Beheshti University of Medical Sciences, Tehran, IR Iran
[2] Clinical Tuberculosis and Epidemiology Research Center, National Research Institute of Tuberculosis and Lung Diseases (NRITLD), Shahid Beheshti University of Medical Sciences, Tehran, IR Iran
[3] Chronic Respiratory Diseases Research Center, National Research Institute of Tuberculosis and Lung Diseases (NRITLD), Shahid Beheshti University of Medical Sciences, Tehran, IR Iran
[4] Department of Biostatistics, Faculty of Medical Sciences, Tarbiat Modares University, Tehran, IR Iran

[*] *Corresponding author*: Seyed Mohammad Reza Hashemian, NRITLD, Shaheed Bahonar Ave, Darabad, P.O:19575/154, Tehran 19569, IR Iran. Tel: +98-9121119279, E-mail: smrhashemian@yahoo.com

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Abstract

Background: Patients admitted to intensive care units have different physiological parameters in comparison with other settings. Changes in cardiovascular and renal functions are characteristics of these patients. An augmented renal clearance (ARC) has been investigated in some groups of critically ill patients, but there are no studies on the occurrence and determinants of ARC in Iran.
Objectives: Our goal was to determine the incidence and associated factors of ARC in Iranian critically ill patients.
Methods: This retrospective cohort study was conducted on patients admitted to the mixed medical-surgical ICU of Masih Daneshvari hospital, Tehran, Iran, as a referral center, during a 3-year period (October 2010 to October of 2012). ARC was defined as creatinine clearance (CLCr) $\geq$ 130 mL/min/1.73 m^2. Two groups were analyzed: medical and surgical admission in ICU.
Results: Augmented renal clearance was present in 184 of 467 Iranian patients (39.4%), and they were young (42.1 $\pm$ 14.6 versus 58 $\pm$ 1 years, P value $<$ 0.01).
Conclusions: In this cohort of Iranian critically ill patients, 39.4% had ARC on admission to the ICU. Augmented renal clearance mainly developed in young Iranian patients.

Keywords: Incidence, Intensive Care Unit, Patients

1. Background

Critically ill patients, compared to outpatient and admitted patients in general care, are a very special population. The physiological functioning of these patients is due to the pathology of the main disease, and the interventions are disrupted.

Changes in renal and cardiovascular functions in these patients are not always easily identifiable through standard diagnostic tests. (1, 2). These patients manifest substantial changes in their renal and cardiovascular function that are not always immediately discernible using standard diagnostic tests (3). Clinicians will commonly assess patients for renal dysfunction.

Renal impairment is clearly confirmed in these individuals; and sometimes, despite the normal concentration of serum creatinine, there may be an increased risk of glomerular titration, which is called renal clearance (ARC).

ARC is a topic recently addressed in critical care medicine and information that evaluates ARC levels in patients (1).

There are data that identify patients at risk of ARC; it can be defined as an altered state that leads to increased clearance of renally eliminated solutes including antibiotics, with the potential for negative effects on patient outcomes.

The plasma of certain amount of matter is cleared, which is measured by the kidneys per unit time.

Although GFR is used to consider ARC easily, a timed urinary creatinine clearance (CLCR) has been most helpful in renal function in patients with a critical illness (1, 4).

Normal CLCR in women and men was 120 mL/min/1.73 m^2 and 130 mL/min/1.73 m^2, respectively.

Udy et al. have employed threshold values of 160 and

150 for men and women, respectively, in brain injury (5, 6). Many studies have used threshold value of 130 to identify ARC. The incidence of ARC varies between different studies depending on different threshold values and special characteristics of the critically ill patients. Maria et al. recorded 28.3% ARC incidence (CLCR> 120 mL/min/1.73 m^2) in critically ill patients on the first day of admission (4), whereas this value for some special patient groups such as septic and traumatized was obtained to be 85.7 and 39.5 (3). Claus et al. studied a cohort of 128 critically ill patients and found that over 50% of the patients had ARC (CrCl > 130 mL/min/1.73 m^2) (7). Risk factors such as age, pregnancy, sepsis, trauma, surgery, or neurosurgery, burns injury, and cystic fibrosis have been introduced for ARC in some studies (5-13).

ARC's epidemiology, risk factors, and clinical characteristics have not been comprehensively investigated in Iran. In this study, we aimed at determining the incidence of ARC on the day of admission in a historical cohort of Iranian critically ill patients at Masih Daneshvari hospital, Tehran, Iran. Also, identifying predictors of ARC was authors' interest.

2. Methods

This retrospective cohort study was conducted on consecutive Iranian patients admitted to the mixed medical-surgical intensive care unit of Masih Daneshvari hospital as a referral center. A total of 467 patients were included in the study during 3 years (October 2010 through October 2012). This cohort was a mixed (medical and surgical) ICU cohort and did not distinguish between admission diagnoses. Exclusion criteria were plasma creatinine levels > 1.3 mg/dL, unavailable 24-hour urine collection, age under 21 years, refusal to participate in the study, and not having a bladder catheter in place. Also, 17 patients were excluded because of incomplete information. Creatinine clearance was calculated from a 24-hour urine collection.

Patients were grouped according to the presence of augmented renal clearance (ClCr $\geq$ 130 mL/min/1.73 m^2). ClCr is estimated with the Cockcroft-Gault formula from creatinine plasma concentrations (estimated ClCr). On admission, demographic data (age, sex, weight, height) were registered. Throughout the following day, acute physiological and chronic health evaluation II (APACHE II), simplified acute physiology score II (SAPS II), and the input/output of fluids were recorded. Additionally, a 24-hour urine sample was collected using a bladder catheter. We measured arterial blood gases, (AVL OMNI 9, Roche Diagnostics, Graz, Austria), plasma and urinary [Na^+], [K^+] and [Cl^-] (Ion selective electrode, AEROSET, Abbott Laboratories, Abbott Park, Illinois, U.S.A), plasma albumin concentration (Bromocresol-sulfoftalein), lactate (Ion selective electrode, AVL OMNI 9), plasma and urinary levels of urea and creatinine (kinetic modification of the Jaffe reaction), and urine proteins. Patients' clinical and physiological data were registered in a questionnaire.

2.1. Statistical Analysis

Continuous variables are expressed as mean with their dispersion coefficients (SD). Qualitative variables are presented as frequencies and percentages. For subgroup comparison, Student's t test was used as indicated. The correlation between continuous variables was established using the Pearson coefficient. A backward conditional logistic regression model was developed to describe risk factors for ARC. The results were analyzed with the SPSS software package version 22.0 (SPSS Inc., Chicago, IL) and SAS version 9.2 statistical software (SAS Institute, Inc). A P value of < 0.05 was considered statistically significant.

3. Results

The main characteristics and results of all patients (n = 469) are demonstrated in Table 1. Overall, in this study, 39.4% of the Iranian patients showed ARC. In medical group, 118 of 317 patients (37.2%), and in surgical group, 66 of 150 patients (44.0%) were identified with ARC. There were 249 (54.8%) males, and the mean age was 53.5 $\pm$ 16.3. Length of ICU stay and hospital length of stay for the medical group was more than surgical group ($P < 0.01$). SAPS II score and APACHE II score were significantly more in the medical group, while CLcr was more in the surgical group ($P = 0.03$). The correlation between CLCr and SAPS II score and APACHE II score were estimated -0.28 and -0.27, respectively ($P < 0.001$), Figure 1 shows this inverse association using linear regression. Differences in demographic, physiological, and laboratory data based on ARC status are provided in Table 2. As illustrated, those manifesting ARC tended to be younger ($P = 0.03$) and male ($P < 0.01$), with lower APACHE II and SAPS II ($P < 0.01$) and higher CLCr ($P = 0.013$) (Figure 2). Backward conditional logistic regression analysis identified younger age as the only independent predictor of ARC (Table 3). For a one-unit increase in age, we expect to see about 16% decrease in the odds of ARC.

4. Discussion

Physicians have not paid enough attention to the ARC issue until now largely due to the limited sensitivity of the standard diagnostic tests and poor awareness of the association of ARC with pharmaceutical medications. Nevertheless, ARC is increasingly being recognized in groups of critically ill patients (1).

Table 1. Laboratory and Demographic Data of the Patients (n = 469)[a]

Variable	Total (n = 467)	Medical (n = 317)	Surgical (n = 150)	P Value
Age, y	53.5 ± 16.3	57.0 ± 17.9	51.9 ± 15.3	0.03
Male gender	249 (54.8)	75 (52.8)	174 (55.8)	0.03
Acute renal failure	68 (15)	33 (23.2)	35 (11.2)	0.06
Urine output, mL/d	2585.0 ± 1827.5	1935.7 ± 1463.2	2910 ± 1001.2	< 0.001
SAPS II	34.0 ± 15.8	42.3 ± 17.1	29.8 ± 13.3	< 0.001
APACHE II score	11.1 ± 6.7	14.8 (7.7)	9.4 (5.4)	< 0.001
M.v.1 h	242 (53.3)	73 (51.4)	169 (54.2)	0.01
M.v.24 - 48	115 (25.3)	87 (61.3)	183 (58.7)	< 0.001
CLCR, mL/min/1.73 m^2	108.5 ± 51.6	107.3 ± 53.0	111.3 ± 50.3	0.03
COPD	23 (5.1)	18 (12.7)	5 (1.6)	< 0.001
Augmented renal clearance	184 (39.4)	118 (37.2)	66 (44.0)	0.03
ICU length of stay, d	8.5 ± 14.7	13.5 ± 20.5	6.1 ± 10.4	< 0.001
Hospital length of stay, d	19.7 ± 17.0	23.7 ± 24.0	17.9 ± 13.8	0.04
Hospital length of stay before ICU, d	6.6 ± 7.6	6.3 ± 10.0	6.8 ± 6.3	0.21

Abbreviations: APACHE II score, acute physiological and chronic health evaluation II; COPD, chronic obstructive pulmonary disease; M.v.1 hour, mechanical ventilation within 1 hour of admission; M.v.24 - 48, mechanical ventilation between 24 - 48 hours; SAPS II, simplified acute physiology score II.
[a]Values are expressed as mean ± SD or No. (%).

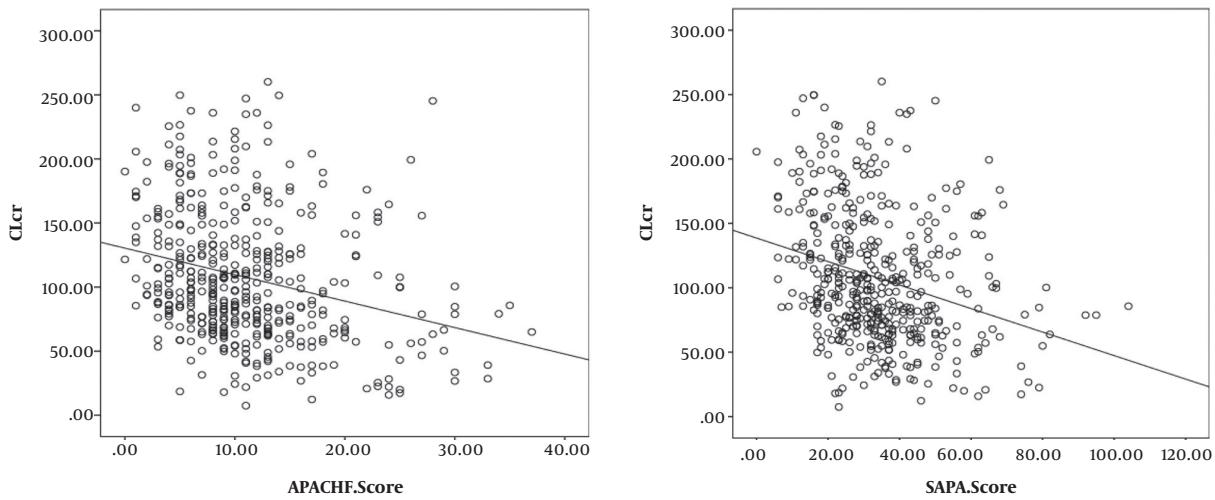

Figure 1. Scatter plot for CLcr and APACHE II and SAPS II score

Also, ARC has not been comprehensively investigated in Iran. The present retrospective cohort study investigated the incidence and associated risk factors of ARC for Iranian critically ill patients. We studied a large cohort of critically ill patients admitted to a mixed medical-surgical ICU during a 3-year period, of whom 39.4 % had augmented renal clearance on the first day of admission; therefore, ARC is almost a frequent condition in the critical care setting at Iran.

ICU patients receive large amounts of fluid and blood products, and they also have some experiences of surgical interventions that lead to high risk of manifesting ARC (1, 8). In this study, 44% of the Iranian patients who were admitted to the ICU on the surgical admission, had ARC, whereas this percent was 37.2% between the patients with medical admission (P = 0.03).

There are well-known conditions that induce ARC such as pregnancy, sepsis, trauma, surgery, or neurosurgery,

Table 2. Demographic, Diagnostic Data in Those with and without ARC[a]

Variable	ARC (n = 184)	Non-ARC (n = 283)	P Value
Age, y	42.1 ± 14.6	58.1 ± 14.2	0.03
Urine output, mL/d	2298.8 ± 1718.7	2704.3 ± 1857.8	< 0.01
Male gender	77 (59.7)	171 (52.8)	< 0.01
APACHE II score	9.3 ± 6.1	11.8 ± 6.8	< 0.01
SAPS II	29.2 ± 15.1	36.1 ± 15.6	< 0.01
CL_{CR}, mL/min/1.73 m^2	174.8 ± 32.0	80.69 ± 28.0	< 0.01
ICU length of stay, d	7.9 ± 12.5	8.7 ± 15.6	0.06
ICU mortality	21.2 (19.1)	19.1 (17.3)	0.04
Hospital mortality	7.2 (8.8)	6.4 (7.1)	0.03
Surgical	90 (69.8)	221 (68.2)	
Medical	39 (30.2)	103 (31.8)	
Renal parameters			
Arterial PH	7.3 (0.1)	7.3 (0.1)	0.90
Arterial PCO_2 mmHg	48.3 (24.2)	44.5 (30.1)	< 0.01
Arterial PO_2, mmHg	109 (80.2)	126.2 (90.6)	< 0.01
Arterial [HCO_3-], mmHg	26.0 (10.0)	23.3 (10.3)	0.05
Plasma [Na+], mEq/L	139.5 (6.0)	141.1 (5.3)	0.06
Plasma [K+], mEq/L	4.3 (0.6)	4.3 (0.7)	0.90
Albumin, g/L	3.4 (0.6)	3.5 (1.8)	0.88

[a]Values are expressed as mean ± SD or No. (%).

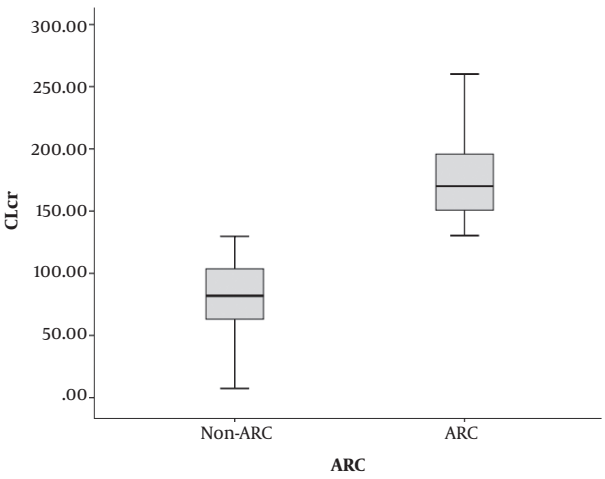

Figure 2. Box plot of CLcr in patients with and without ARC

Table 3. Logistic Regression Analysis with ARC as the Outcome Variable

Variable	OR	95%CI	P Value
Age	0.84	0.79 - 0.89	< 0.001

Abbreviations: OR, odds ratio; 95%CI - 95%, confidence interval.

burns injury, and cystic fibrosis. We found Iranian patients were significantly younger, this finding was similar to some previous researches (3, 8, 9, 14, 15). It was also demonstrated that patients with a lower APACHE II and SAPSII score are at high risk of obvious ARC, however, they were not entered as predictors in to a backward conditional regression model. We found no differences in patients with and without ARC in arterial blood gases (ABG), except for $Paco_2$ and Pco_2, which was similar to the results obtained in other studies (15-17). The strong point of this study was a large sample size. For future studies on ARC, it is highly recommended to investigate new approaches to drug dosing in populations of Iranian ICU patients.

4.1. Conclusions

In this cohort of Iranian critically ill patients, 39.4% of the patients had ARC on admission to the ICU. Augmented renal clearance mainly developed in young Iranian patients.

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Footnotes

Authors' Contribution: Seyed Mohammad Reza Hashemian performed the design, coordinated the study, and prepared the manuscript. Batoul Khoundabi gave technical advice on statistical modeling and revised the manuscript.

Conflict of Interests: There is no conflict of interest in this study.

Financial Disclosure: There is no financial disclosure.

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